

Claims

1. A pharmaceutical composition for treating immunological disorders by inhibiting activation of T lymphocytes, comprising, as active ingredients, two or more selected from the group consisting of : a substance capable of blocking binding of an MHC Class II molecule and a receptor thereof, a substance capable of blocking binding of a costimulatory molecule and a receptor thereof, a substance capable of blocking binding of an adhesion molecule and a receptor thereof, and a substance capable of blocking binding of a cytokine and a receptor thereof.

2. The pharmaceutical composition for treating immunological disorders according to claim 1, wherein the substance capable of blocking the binding of the MHC Class II molecule and CD4 is selected from the group consisting of (1) an antibody to the MHC Class II molecule; (2) a simple fusion monomeric protein formed by linkage of a soluble extracellular domain of LAG3 to a hinge region of an Fc fragment of an immunoglobulin molecule; (3) a simple fusion dimeric protein in which two molecules of the simple fusion monomeric protein are joined by intermolecular disulfide bonds in the hinge region; (4) a concatameric fusion monomeric protein formed by linkage of an N-terminus of a soluble extracellular domain of the LAG3, linked to the hinge region of the simple fusion monomeric protein, to a C-terminus of a soluble extracellular domain of another LAG3 molecule; (5) a concatameric fusion dimeric protein in which two molecules of the concatameric fusion monomeric protein are joined by intermolecular disulfide bonds in the hinge region; and (6) glycosylated forms of the proteins according to (2) to (5).

3. The pharmaceutical composition for treating immunological disorders according to claim 1, wherein the costimulatory molecule is B7, CD154, CD70, OX40L, ICOS-L, 4-1BBL, HVEM,

FASL or PDL, and the receptor thereof is CD28 and CTLA4, CD40, CD27, OX40, ICOS, 4-1BB, LIGHT, FAS or PD-1.

4. The pharmaceutical composition for treating immunological disorders according to claim
5 3, wherein the substance capable of blocking the binding of the B7 molecule and the CD28 is selected
from the group consisting of (1) an antibody to the B7 molecule; (2) a simple fusion monomeric protein
formed by linkage of a soluble extracellular domain of the CTLA4 to a hinge region of an Fc fragment
of an immunoglobulin molecule; (3) a simple fusion dimeric protein in which two molecules of the
simple fusion monomeric protein are joined by intermolecular disulfide bonds in the hinge region; (4) a
10 concatameric fusion monomeric protein formed by linkage of an N-terminus of a soluble extracellular
domain of the CTLA4, linked to the hinge region of the simple fusion monomeric protein, to a C-
terminus of a soluble extracellular domain of another CTLA4 molecule; (5) a concatameric fusion
dimeric protein in which two molecules of the concatameric fusion monomeric protein are joined by
intermolecular disulfide bonds in the hinge region; and (6) glycosylated forms of the proteins according
15 to (2) to (5).

5. The pharmaceutical composition for treating the immunological disorder according to
claim 1, wherein the adhesion molecule is LFA-3, ICAM-1 or VCAM-1, and the receptor thereof is
CD2, LFA-1 or VLA-4.

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6. The pharmaceutical composition for treating immunological disorders according to claim
5, wherein the substance capable of blocking the binding of the LFA-3 and the CD2 is selected from the
group consisting of (1) an antibody to the LFA-3; (2) a simple fusion monomeric protein formed by
linkage of a soluble extracellular domain of the CD2 to a hinge region of an Fc fragment of an
25 immunoglobulin molecule; (3) a simple fusion dimeric protein in which two molecules of the simple

fusion monomeric protein are joined by intermolecular disulfide bonds in the hinge region; (4) a concatameric fusion monomeric protein formed by linkage of an N-terminus of a soluble extracellular domain of the CD2, linked to the hinge region of the simple fusion monomeric protein, to a C-terminus of a soluble extracellular domain of another CD2 molecule; (5) a concatameric fusion dimeric protein in which two molecules of the concatameric fusion monomeric protein are joined by intermolecular disulfide bonds in the hinge region; and (6) glycosylated forms of the proteins according to (2) to (5).

7. The pharmaceutical composition for treating immunological disorders according to claim 1, wherein the cytokine is IL-1, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, TNF, TGF, IFN, GM-CSF, G-CSF, EPO, TPO or M-CSF, and the receptor thereof is IL-1R, IL-2R, IL-3R, IL-4R, IL-5R, IL-6R, IL-7R, TNFR, TGFR, IFNR, INF- α R, - β R and - γ R, GM-CSFR, G-CSFR, EPOR, cMpl or gp130.

8. The pharmaceutical composition for treating immunological disorders according to claim 7, wherein the substance capable of blocking the binding of the TNF and the TNFR is selected from the group consisting of (1) an antibody to the TNF; (2) a simple fusion monomeric protein formed by linkage of a soluble extracellular domain of the TNFR to a hinge region of an Fc fragment of an immunoglobulin molecule; (3) a simple fusion dimeric protein in which two molecules of the simple fusion monomeric protein are joined by intermolecular disulfide bonds in the hinge region; (4) a concatameric fusion monomeric protein formed by linkage of an N-terminus of a soluble extracellular domain of the TNFR, linked to the hinge region of the simple fusion monomeric protein, to a C-terminus of a soluble extracellular domain of another TNFR molecule; (5) a concatameric fusion dimeric protein in which two molecules of the concatameric fusion monomeric protein are joined by intermolecular disulfide bonds in the hinge region; and (6) glycosylated forms of the proteins according to (2) to (5).

9. The pharmaceutical composition for treating immunological disorders according to any one of claims 1 to 8, wherein the immunological disorder is an autoimmune disease or a transplantation rejection.

5 10. The pharmaceutical composition for treating immunological disorders according to claim 9, wherein the autoimmune disease is selected from the group consisting of rheumatoid arthritis, multiple sclerosis, myasthenia gravis, Grave's disease, Hashimoto's thyroiditis, Addison's disease, vitilligo, scleroderma, Goodpasture syndrome, Becet's disease, Crohn's disease, ankylosing spondylitis, uveitis, thrombocytopenic purpura, pemphigus vulgaris, childhood diabetes, autoimmune anemia,
10 cryoglobulinemia, adrenoleukodystrophy (ALD), and systemic lupus erythematosus (SLE).